

Claims

1. A DNA base sequencing method in which pyrophosphate produced upon synthesizing a strand complementary to a template DNA is converted into ATP, which is reacted with luciferine in the presence of an enzyme such as luciferase, and the complementary strand synthesis is monitored by detecting the resulting chemiluminescence to obtain DNA sequence information, said method being characterized by comprising supplying four kinds of dNTP into the reaction vessel by pressurizing via independent capillaries or narrow grooves which can be in contact with a reaction solution.

2. The method according to claim 1, characterized in that each dNTP is supplied in a previously designated order into the reaction vessel by pressurizing each dNTP reservoir in order.

3. A system to obtain DNA sequence information in which pyrophosphate produced upon synthesizing a strand complementary to a template DNA is converted into ATP which is reacted with luciferine in the presence of an enzyme such as luciferase and the complementary strand synthesis is monitored by detecting the resulting chemiluminescence, said system being characterized by comprising a means for supplying four kinds of dNTP into a reaction vessel via independent capillaries or narrow grooves which can be in contact with a reaction solution, by pressurizing or by a liquid transfer system.

4. The system according to claim 3, characterized in that the reaction vessel and the dNTP-supply capillaries or

narrow grooves are incorporated into one module as a unit.

5. The system according to claim 3, characterized in that the dNTP-supply capillaries or narrow grooves can be introduced into the reaction solution from the top of the reaction vessel.

6. The system according to claim 3, characterized in that dNTP is supplied intermittently and repeatedly into the reaction vessel by controlling pressurization of each dNTP reservoir or by controlling an electric field between each dNTP reservoir and the reaction vessel in addition to the pressurization.

7. A reaction chamber module used in the system according to claim 3, characterized by comprising at least one reaction vessel and at least four lines of capillaries or narrow grooves for reagent introduction corresponding to four kinds of dNTP; said capillaries or narrow grooves having an inner diameter of less than 0.2 mm and/or a cross section area of less than 0.04 mm², at the inlet of the reaction vessel.

8. A reaction chamber module used in the system according to claim 3, characterized by comprising at least one reaction vessel and at least four lines of capillaries or narrow grooves for reagent introduction corresponding to four kinds of dNTP; said capillaries or narrow grooves having an inner diameter of less than 0.1 mm and/or a cross section area of less than 0.01 mm², at the inlet of the reaction vessel.

9. The reaction chamber module according to claim 7,

characterized in that dNTP-containing reaction reagents can be introduced from reagent reservoirs into the reaction vessel via capillaries or narrow grooves at the bottom of the reaction vessel.

10. The reaction chamber module according to claim 7, characterized in that a supply unit for dNTP-containing reaction reagents and the reaction vessel unit are separable and each reaction agent is alternately and repeatedly supplied from the reaction reagent supply unit installed on the top of the reaction vessel into each reaction solution via capillaries or narrow grooves.

11. A DNA sequencing method in which pyrophosphate produced upon synthesizing a strand complementary to a template DNA is converted into ATP which is reacted with luciferine in the presence of an enzyme such as luciferase and the complementary strand synthesis is monitored by detecting the resulting chemiluminescence to obtain DNA sequence information,

said method being characterized in that a primer which sets a starting point of the complementary strand synthesis is immobilized onto a solid surface, pyrophosphate produced upon synthesizing DNA complementary strand which is hybridized with the primer is converted into ATP which is reacted with luciferine by luciferase or the like, and the DNA base sequence is monitored by detecting the resulting chemiluminescence.

12. The method according to claim 11, characterized in that different kinds of primers which hybridize with the target DNA are immobilized onto different solid surfaces or different cells having sectioned solid surfaces, the

designated reaction is carried out using dNTP after hybridization with the target DNA, and chemiluminescence resulting from the complementary strand synthesizing reaction caused by different primers is distinguished to monitor the sequence.

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13. The method according to claim 11, characterized in that the primers are independently immobilized onto the surface of beads which are spatially separated according to the kind of primer.

14. The method according to claim 11, characterized in that the solids with the immobilized primers on their surface are held in cells which are spatially separated according to the kind of primer.

15. A DNA analyzing system which is used in the method of claim 11.

16. The DNA analyzing system according to claim 15, characterized in that said system is a detection system capable of distinguishing the position of the chemiluminescence emission.

17. The DNA analyzing system according to claim 15, characterized in that the chemiluminescence is detected by an area sensor such as a cooled CCD.

18. The DNA analyzing system according to claim 15, characterized in that the means for detecting chemiluminescence comprises a chemiluminescence detecting device, such as a photon multiplier tube and an avalanche photodiode, and a system in which the

position of the reaction vessel is shiftable relative to the detecting device.

19. The DNA analyzing system according to claim 15, characterized in that reagents can be supplied without contact with the reaction vessel.

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20. The DNA analyzing system according to claim 15, characterized in that reagents are simultaneously supplied independently to different reaction vessels by an ink jet method.

21. The DNA analyzing system according to claim 15, characterized in that reagents are supplied to the reaction vessel via capillaries having a diameter of less than 0.2 mm.

22. A system characterized in that a DNA to be used as a template for complementary strand synthesis is immobilized onto a solid surface, pyrophosphate produced upon synthesizing complementary strand which is hybridized with the DNA is converted into ATP which is reacted with luciferine by luciferase or the like, and the DNA base sequence is monitored by detecting the resulting chemiluminescence, said system being characterized by comprising a means to remove primers and complementary strand synthesis products or to stop the extension reaction by adding ddNTPs into the reaction chambers followed by removing ddNTPs after the first sequencing process using the primers, to freshly inject primers and enzymes or the like, and to subsequently carry out the second DNA sequencing process, and providing a means to carry out this process repeatedly, if necessary.

23. The system according to claim 22, characterized by comprising a means in which different kinds of target DNAs (DNA samples) are immobilized onto different solid surfaces or sectioned different cells, the designated reaction is carried out using enzymes and dNTP after hybridization with the primers, and chemiluminescence resulting from the complementary strand synthesizing reaction caused by different primers is distinguished to monitor the sequence.

24. A DNA base sequencing system, characterized by comprising a reaction vessel, reagent reservoirs each holding any one of four kinds of dNTP, means to supply dNTP into the reaction vessel at least partly consisting of a capillary or a narrow groove, pressurizing means to control the supply of the reagents, means to detect chemiluminescence emitted from the reaction vessel, and means to analyze data to obtain DNA sequence information by processing the detected data.

25. The method according to claim 1, wherein the same kind of dNTP is added twice to assure that the reaction proceeds thoroughly.

26. The system according to claim 1, wherein the same kind of dNTP is added twice to assure that the reaction proceeds thoroughly.